REMARKS

Claims 22-37 were pending in this application. In order to expedite prosecution and without conceding to the propriety of the rejections, claims 22, 23, 24 and 37 have been amended and claims 25, 29, and 33 have been canceled without prejudice to Applicant's right to pursue the subject matter of the canceled claims in related applications. In addition, new claims 38-51 have been added.

New independent claim 38 recites a method for inhibiting colon cancer cell growth in a human, comprising administering to a human in need of such treatment an effective amount of a composition comprising specific polymethoxylated flavones. New independent claim 39 recites a method for inhibiting development of colon cancer in a human, comprising administering to a human in need of such treatment an effective amount of a composition comprising specific polymethoxylated flavones. Dependent claims 40, 43, and 46-48 recite the type or form of the composition administered to the human subject. Dependent claims 41, 42, 44 and 45 recite the amount of the composition administered to the human subject. Dependent claims 49 and 51 recite that the method for preventing or treating colon cancer further comprises administering to the human subject a rosemary extract, a black tea extract, a Mexican Bamboo extract or a Huzhang extract. Dependent claim 50 recites that the method for preventing or treating colon cancer further comprises administering to the human subject resveratrol, hydroxylated analogs of resveratrol, methoxylated analogs of resveratrol.

Support for the amendments to claims and new claims can be found throughout the specification, see *e.g.*, the specification at page 2, line 33 to page 3, line 5, page 3, lines 22-23, page 7, lines 17-21, page 9, line 8 to page 10, line 21, and page 11, line 9 to page 21, line 21. The amendments and new claim are fully supported by the specification of the present application and do not constitute new matter. Upon entry of this Amendment, claims 22-24, 26-28, 30-32, and 34-51 will be pending and under examination.

Applicants respectfully request that the amendments and remarks made herein be entered into the record of the application and fully considered by the Examiner.

1. INTERVIEW SUMMARY

Applicants thank Examiner Srivastava for granting the telephonic interview with Applicants' attorney, Jennifer Chheda, on January 19, 2006 to discuss the outstanding Office Action in the present application. In particular, Applicants' attorney requested Examiner Srivastava clarify the priority statements and enablement rejections in the Office Action.

Examiner Srivastava informed Applicants' attorney that he would consider Applicants' written response to the Office Action.

2. INFORMATION DISCLOSURE STATEMENT

Applicants acknowledge that the Examiner has considered and made of record references A01-A07, B01-B30, C01-C18, C20-C31, C33-C46, and C48-C54. Applicants note that references C19 and C32 were not considered because the references are not in the English language. Applicants also note that reference C47 was not considered since the reference was incomplete. Applicants submit herewith a complete copy of reference C47. To ensure that reference C47 is considered, Applicants have submitted the copy of the reference along with a Supplemental Information Disclosure Statement and revised PTO-1449 form. Applicants respectfully request that the Examiner consider and make reference C47 of record in the present application.

3. ENTITLEMENT TO PRIORITY

The Examiner contends that Applicants are not entitled to the priority benefit of U.S. provisional application Serial No. 60/155,018, filed September 21, 1999 and International application No. PCT/US00/25733, filed September 20, 2000. Applicants note that the present application is a national stage application of International application No. PCT/US00/25733, filed September 20, 2000. Thus, the specification of International application No. PCT/US00/25733 is, and, in fact, must be, identical to the specification of the present application. Accordingly, the present application is, at minimum, entitled to the priority benefit of September 20, 2000.

4. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN

Claims 22-37 are rejected under 35 U.S.C. § 112, first paragraph, as not enabled for their full scope by the specification. Applicants acknowledge that the Examiner recognizes that the specification enables, *inter alia*, a method to treat colon cancer via administering a composition containing the 14 recited orange peel extract polymethoxylated flavones (July 27, 2005 Office Action, page 4, paragraph 14). Applicants note that pending claim 22 and dependent claims 26-28, 30-32, 34-37 and 49 are directed to such a method However, the Examiner contends that the specification does not reasonably enable methods for preventing colon cancer via administering a composition comprising the 14 recited orange peel extract

polymethoxylated flavones. The Examiner also contends that the specification does not reasonably enable methods for preventing or treating colon cancer via administering a composition comprising the 14 recited orange peel extract polymethoxylated flavones and extracts of other plants, other phytochemicals or resveratrol. For the reasons detailed below, the rejections under 35 U.S.C. § 112, first paragraph, cannot stand and should be withdrawn.

The test for enablement is whether one of skill in the art could make and use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Teletronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). The specification preferably omits well known subject matter. *See Hybritech v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well known in the art."). Further, one skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. See *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990) ("A decision on the issue of enablement requires determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention." *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278, 1291 (D. Del. 1991); *see also DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985).

Accordingly, the law does not require the scope of enablement provided by the specification to mirror precisely the scope of protection sought by the claims. *See In re Fisher* , 166 USPQ 18, 24 (C.C.P.A. 1970); *see also In re Wright*, 27 USPQ2d 1510 (Fed. Cir. 1993). To be enabled, all the law requires is that the scope of enablement provided by the specification bear a "reasonable correlation" to the scope of the claims. *Id.* Moreover, even if evidence to doubt the proposed correlation exists, " the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition." *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995). Thus, to support a non-enablement rejection, the Examiner must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate the teaching in the specification across the entire scope of the claims. *Id.*

In addition, the Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of non-enablement. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971); MPEP § 2164.02. A patent applicant's specification which contains a teaching of how to

make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *Id.*

Applicants respectfully assert that the specification coupled with information known to the skilled artisan as of the effective filing date of the present application would have provided sufficient guidance to enable one of skill in the art to practice the claimed invention without undue experimentation. The specification of the present application teaches methods for preventing and treating colon cancer by administering a composition comprising the 14 recited polymethoxylated flavones. Moreover, the specification provides *in vitro* and *in vivo* assays for determining the efficacy of a composition comprising the specific polymethoxylated flavones recited in the pending claims, alone or in combination with the extracts or compounds recited in claims 37 and 49-51, for the prevention and treatment of colon cancer (see, *e.g.*, page 4, line 27 to page 7, line 21 and page 8, line 17 to page 9, line 7).

In addition, the specification provides *in vivo* data from two experiments in an art-accepted mouse colon cancer model demonstrating that a composition comprising the specific polymethoxylated flavones recited in the pending claims is efficacious in the prevention of colon cancer. The *in vivo* data from the first experiment demonstrates that the administration of a composition comprising the polymethoxylated flavones recited in the pending claims reduces the formation of aberrant crypt (AC) and aberrant crypt foci (ACF), which are biomarkers for colon cancer, in female CF-1 mice injected with the carcinogen azoxymethane (AOM) (see the specification at page 5, line 7 to page 6, line 30). In the experiment, the mice were administered a composition comprising the specific polymethoxylated flavones two weeks before the first AOM injection and throughout the experiment. The administration of the composition to the mice reduced the number of aberrant crypt and aberrant crypt foci induced by the AOM injection. In other words, the composition comprising the polymethoxylated flavones recited in the pending claims prevented the formation of aberrant crypt and aberrant crypt foci, a measurement of the efficacy of a composition to prevent colon cancer.

The *in vivo* data from the second experiment in the specification demonstrates that the administration of a composition comprising the polymethoxylated flavones recited in the pending claims reduces tumor formation in female CF-1 mice injected with the carcinogen AOM (see the specification at page 6, line 31 to page 7, line 21). In the experiment, the mice were administered a composition comprising the specific polymethoxylated flavones two weeks before the first AOM injection and throughout the experiment. The administration of the composition to the mice reduced the number of colon tumors induced by the AOM injection to the same extent as the positive control, nordihydroxyguaiaretic acid (NGDA),

i.e., a compound known to be useful in the prevention of colon cancer. In other words, the composition comprising the polymethoxylated flavones recited in the pending claims prevented the formation of tumors in the colon, and thus, prevented colon cancer. Accordingly, Applicants respectfully assert that the specification does, indeed, enable one of skill in the art, without undue experimentation, to prevent colon cancer by practicing the claimed methods of the invention.

Applicants respectfully assert that the specification coupled with information known to the skilled artisan as of the effective filing date of the present application regarding a composition comprising the recited polymethoxylated flavones, and the compounds and extracts recited in claims 37 and 49-51 would have provided sufficient guidance to enable one of skill in the art to practice the methods of claims 37 and 49-51 without undue experimentation. As discussed *supra*, the specification of the present application teaches methods for treating and preventing colon cancer by administering a composition comprising the 14 recited polymethoxylated flavones and the compounds or extracts recited in claims 37 and 49. The specification also provides *in vitro* and *in vivo* assays for determining the efficacy of such a composition for the treatment and prevention of colon cancer. Moreover, the specification also provides *in vitro* and *in vivo* data regarding the efficacy of resveratrol for the prevention and treatment of cancer (see the specification at page 12, line 4 to page 13, line 20). As stated in the specification of the present application, Mexican Bamboo and Huzhang contain high amounts of resveratrol. In addition, the specification provides a discussion of references published prior to the effective filing date of the present application that describe the utility of the recited compounds and extracts for the prevention and treatment of cancer (see the specification at page 13, line 21 to page 14, line 10). Thus, Applicants respectfully assert that one of skill in the art would be able to determine the amounts of the recited polymethoxylated flavones and the recited compounds or extracts to include in a composition for use in the treatment and/or prevention of colon cancer and the method of administration of such a composition, without undue experimentation.

Thus, the specification coupled with the information known as of the effective filing date of the present application would have enabled one of skill in the art to practice the claimed methods of the invention without undue experimentation. Accordingly, Applicants submit that the pending claims are fully enabled for the scope of the claimed subject matter.

In view of the foregoing, Applicants respectfully assert that the rejections under 35 U.S.C. § 112, first paragraph, for lack of enablement cannot stand and should be withdrawn.

5. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

Claims 22-37 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard the invention. For the reasons detailed below, the rejections under 35 U.S.C. § 112, second paragraph, cannot stand and should be withdrawn.

The Examiner contends that claims 22 and 23 are indefinite because the phrase "such that" is vague and unclear. Applicants respectfully assert that one of skill in the art would appreciate that the phrase "such that the colon cancer is treated" recited in claim 22 means that the administration of an effective amount of the composition treats the colon cancer in the human subject. Similarly, Applicants respectfully assert that one of skill in the art would appreciate that the phrase "such that the colon cancer is prevented" recited in claim 23 means that the administration of an effective amount of the composition prevents the colon cancer in the human subject. However, in order to expedite the prosecution of the application and without conceding to propriety of the rejection, Applicants have amended claims 22 and 23 to delete the phrases "such that the colon cancer is prevented" and "such that the colon cancer is prevented".

The Examiner contends that claim 24 is indefinite because of the phrase "in a reduction in" is vague and unclear. Applicants have amended claim 24 to recite that the administration of the composition results in a reduction in the formation of aberrant crypt or aberrant crypt foci in the human. Applicants respectfully assert that one of skill in the art would appreciate that formation of aberrant crypt or aberrant crypt foci is reduced in the human subject administered an effective amount of the composition of the claimed invention.

The Examiner contends that claims 25, 28, 29, and 31-33 are indefinite because of the recitation of the phrases "20-50 μg/ml", "5000 ppm supplement of the human's diet", and "0.2% of the human's diet". In order to expedite prosecution of the present application and without conceding to the propriety of the rejection, Applicants have canceled claims 25, 29, and 33, without prejudice to Applicants' right to pursue the canceled subject matter in a related application(s). Applicants respectfully assert that one of skill in the art would be able to ascertain the amount of the composition of the claimed invention administered to the human subject to prevent or treat colon cancer from the recitation of the phrases "5000 ppm supplement of the human's diet" and "0.2% of the human's diet". For example, one of skill

would determine the human's diet and administer an amount of the composition of the claimed invention that is equivalent to 0.2% of the human's diet.

The Examine contends that claim 37 is indefinite because the recitation of the term "extract" is vague. Applicants have amended claim 37 to delete the recited extracts and added new dependent claim 49 that recites a composition comprising the specific polymethoxylated flavones and rosemary extract, black tea extract, Mexican Bamboo extract or Huzhang extract. The term "extract" is a commonly understood term and is used in the art. Applicants respectfully assert that given the discussion in the specification regarding the use of such extracts for the prevention and treatment of cancer and the state of the art as of the effective filing date of the present application regarding such extracts, one of skill in the art would be able ascertain the metes and bounds of such extracts.

In view of the foregoing, Applicants respectfully assert that the rejections under 35 U.S.C. § 112, second paragraph, cannot stand and should be withdrawn.

6. THE REJECTION UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

Claims 22-24 are rejected under 35 U.S.C. § 102(b) as anticipated by Xu et al., 1993, European Journal of Cancer Prevention 2: 327-335 (hereinafter "Xu"). The Examiner contends that Xu teaches "treating colon cancer as manifested by reduction in the quantities of urinary excretion of N-nitrosoproline (NPRO) in subjects treated with orange peel powder ..." For the reasons detailed below, the rejection cannot stand and should be withdrawn.

The legal test for anticipation under 35 U.S.C. § 102 requires that each and every element of the claimed invention be disclosed in a prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the public in possession of the invention. *W.L. Gore Associates v. Garlock, Inc.* , 721 F.2d 1540, 1554 (Fed. Cir. 1983); *In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985).

Contrary to the Examiner's contention, Xu does not teach treating colon cancer by administering orange peel powder. Rather, Xu teaches that administration of orange peel powder (6g, containing 3 mg vitamin C) together with 300 mg of L-proline to human subjects from a high-risk area for *gastric* cancer decreased urinary levels of N-nitrosoproline (NPRO) relative human subjects administered nothing or 300 mg of L-proline (see Figure 3 of Xu on page 332). The effect of orange peel powder on the levels of urinary NPRO between human subjects with normal gastric mucosa or superficial gastritis, human subjects with moderate or severe intestinal metaplasia, and human subjects with moderate/severe dysplasia were not significantly different (see the abstract on page 327 and Figure 3 of Xu on page 332). Based

upon the experimental results, Xu suggests that regular consumption of fruits and fresh vegetables rich in the compounds tested, including orange peel powder, "...is probably the most effective measure for the prevention of *gastric* carcinogenesis in humans" (Xu at page 334, 1st column). Thus, Xu describes the effect that orange peel powder has on the urinary excretion of NPRO by human subjects at high risk of *gastric* cancer and suggests consuming fruits and vegetables containing orange peel powder to prevent *gastric* carcinogenesis. As the Examiner is aware, gastric cancer is stomach cancer. Therefore, Xu does not teach or suggest the use of orange peel powder to prevent or treat colon cancer, much less a composition comprising the 14 specific polymethoxylated flavones recited in the pending claims. Accordingly, Xu does not anticipate the claimed invention.

In view of the foregoing, Applicants assert that the rejection under 35 U.S.C. § 102(b) that the rejection be withdrawn.

7. THE REJECTION UNDER 35 U.S.C. § 103 SHOULD BE WITHDRAWN

Claims 22-37 are rejected under 35 U.S.C. § 103(a) as obvious over combined teachings from Xu in view of Bailey *et al.*, U.S. Patent No. 5,859,293 (hereinafter "Bailey"), Madis Botanicals, Inc. Resverapure™ Resveratrol PE 8% Product Code 04544, page 2, lines 6-7 and 15-31, 1997 (hereinafter "Madis Botanicals"), and The Healing Herbs, The Ultimate Guide to the Curative Power of Nature's Medicine, 1991, Rodale Press, Emmaus, PA, page 349, column 2, lines 3-10 (hereinafter "Castleman"). The Examiner contends that: (i) Xu teaches "treating colon cancer as manifested by reduction in the quantities of urinary excretion of N-nitrosoproline (NPRO) in subjects treated with orange peel powder ..."; (ii) Bailey teaches "...inhibition or delayed onset of certain types of cancers when extracts from rosemary and other plants are ingested"; (iii) "Madis Botanicals ... teaches powdered nutraceutical and dietary supplement preparations of resveratrol obtained from Huzhang or knotweed to inhibit carcinogenesis or tumerogenesis"; and (iv) "Castleman teaches that black tea has antioxidants and therefore, it may also be helpful in cancer prevention." The Examiner contends that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to combine the specific polymethoxylated flavones and the compounds or extracts in a composition and to administer the composition for the treatment of cancer. For the reasons detailed below, the rejection cannot stand and should be withdrawn.

A finding of obviousness requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere* 383 U.S. 1 (1996). The proper inquiry is whether the art suggests the invention, and whether the art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O 'Farrell* 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Applicants' disclosure. *In re Vaeck* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

None of the cited references teach or suggest the currently claimed methods. As discussed *supra*, Xu does not teach or suggest administering orange peel powder to treat or prevent colon cancer, much less a composition comprising the 14 specific polymethoxylated flavones recited in the pending claims and resveratrol, hydroxylated analogs of resveratrol, methoxylated analogs of resveratrol, a rosemary extract, a black tea extract, a Mexican Bamboo extract or a Huzhnag extract.

The deficiencies of Xu are not cured by Bailey, Madis Botanicals or Castleman, either alone or in combination. In particular, none of the references, either alone or in combination, teach or suggest methods of preventing or treating colon cancer in a human subject by administering to a human in need thereof an effective amount of a composition comprising the polymethoxylated flavones recited in the pending claims, alone or in combination with resveratrol, hydroxylated analogs of resveratrol, methoxylated analogs of resveratrol, a rosemary extract, a black tea extract, a Mexican Bamboo extract or a Huzhnag extract.

Accordingly, Applicants submit that the cited references do not render the pending claims obvious.

In view of the foregoing, Applicants assert that the rejection under 35 U.S.C. § 103(a) that the rejection be withdrawn.

8. DOUBLE PATENTING REJECTION SHOULD BE HELD IN ABEYANCE

Claims 22-37 are provisionally rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 39, 43, 63, 71 and 72 of co-pending U.S. patent application Serial No. 09/992,860 (hereinafter "the '860 application").

Applicants respectfully request that the double patenting rejection be held in abeyance until such time as there is allowable subject matter, at which time the matter will be revisited in light of allowable subject matter.

CONCLUSION

Applicants believe that the present claims meet all the requirements for patentability. Entry of the foregoing amendments and remarks into the file of the application is respectfully requested. Withdrawal of all rejections and consideration of the amended and new claims are requested.

If any issues remain, the Examiner is urged to telephone the undersigned.

Respectfully submitted,

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